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**Sprouty genes regulate proliferation and survival of human embryonic stem cells.**

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**Public Summary:**

Sprouty genes are regulators of signaling pathways that are important in hESCs. In this paper, we showed that the Sprouty genes have important functions in hESCs, including regulation of self-renewal.

**Scientific Abstract:**

Sprouty (Spry) genes encode negative regulators of receptor tyrosine kinase (RTK) signaling, which plays important roles in human embryonic stem cells (hESCs). SPRY2 and SPRY4 are the two most highly expressed Sprouty family members in hESCs, suggesting that they may influence self-renewal. To test this hypothesis, we performed siRNA-mediated knock down (KD) studies. SPRY2 KD resulted in increased cell death and decreased proliferation, whereas SPRY4 KD enhanced survival. In both cases, after KD the cells were able to differentiate into cells of the three germ layers, although after SPRY2 KD there was a tendency toward increased ectodermal differentiation. SPRY2 KD cells displayed impaired mitochondrial fusion and cell membrane damage, explaining in part the increased cell death. These data indicate that Sprouty genes regulate pathways involved in proliferation and cell death in hESCs.

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